SIMULATION-BASED TEACHING AND LEARNING FOR ELECTROPHYSIOLOGY BY iCELL

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Abstract—An interactive cell modeling web site, iCell (http://ssd1.bme.memphis.edu/icell/), that integrates research and education, was developed as a simulation-based teaching and learning tool for electrophysiology. The site consists of JAVA applets representing models of various cardiac cells and neurons, and provides simulation data of their bioelectric activities at cellular level. Each JAVA-based model allows the user to go through menu options to change model parameters, run and view simulation results. The site also has a glossary section for the scientific terms. iCell has been used as a teaching and learning tool for four graduate courses at the Joint Biomedical Engineering Program of University of Memphis and University of Tennessee. This modeling tool was also used as a collaboration site among our colleagues interested in simulations of cell membrane activities. Scientists from the fields of biosciences, engineering, life sciences and medical sciences in USA, Canada, China, Brazil, England, Ireland, the Netherlands, New Zealand, Spain and Turkey have tested and utilized iCell as a simulation-based teaching, learning and collaboration environment. The platform-independent software, iCell, provides us with an interactive and user-friendly teaching and learning tool, and also a collaboration environment for electrophysiology to be shared over the Internet.
Keywords—simulation data, computational models, single cell membrane models

I. INTRODUCTION

The interactive cell modeling tool, iCell, integrates research and education for electrophysiology and is located at http://ssd1.bme.memphis.edu/icell/. The site consists of JAVA applets representing models of various cardiac cells and neurons, and provides simulation data of their bioelectric activities at single cell level. Each JAVA-based model gives an overview of the cell, illustrates the cell membrane with an electrical equivalent circuit and cites the published modeling paper for further information. The cell models in iCell are grouped into versions, and cardiac or neuron "modelboxes". The Cardiac Modelbox has the applets for cardiac electrophysiology and these applets are for (1) a rabbit sinoatrial node cell model (Demir *et al*, 1994), (2) guinea pig ventricular cell model (Luo and Rudy, 1991), (3) rabbit atrial cell model (Lindblad *et al,* 1997), and (4) human atrial cell model (Nygren *et al*, 1998). Currently, the applets in the Neuron Modelbox are for (1) a squid axon model (Hodgkin and Huxley, 1952) and (2) an Aplysia R15 bursting neuron model (Demir *et al,* 1997). Each JAVA-based model allows the user to go through menu options to change model parameters or conditions, run and view simulation results. iCell also has a glossary section for the scientific terms to overcome the language problem among the scientists from different disciplines.

II. MODEL DEVELOPMENT IN JAVA

The iCell models were presented as JAVA applets in HTML pages and can be executed in any JAVA-enabled browser. All of these JAVA applets were developed under JDK1.2 (Java Development Kit) of Sun Microsystems Inc. Each applet has a user-friendly interface and allows the user to go through menus to choose simulation protocols, change model parameters, run simulations, select and view the simulation data.

All of the JAVA applets have the similar structure. There are two classes in each of the JAVA applets. The first class is for the interface layout, GUI design and action handling; such as, where the figures will be graphed in the whole window, where the buttons are, and what should be done if the user pushes a button, etc. The second class is used to calculate the model results and to graph the area. All the ordinary differential equations (ODEs) are solved in the second class. The calculated data are stored in arrays and are graphed in the proper area. The second class will also handle “mouse down” action. When the user clicks on the figure in the window, the applet will display the exact coordinates that the mouse points to.

The Uniform Resource Locator (URL) technique is used in the applet for the Aplysia R15 bursting neuron. The

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Abstract

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simulations for this neuron can take the longest and the data saved may be very big too. Thus, this applet gives the user the option of running simulations or viewing the pre-calculated simulation results. With the URL technique, the pre-calculated simulation data results were saved in our web server. If the user would like to view these results, then he chooses the simulation file to view and the results are displayed in the web browser instantly.

III. TEACHING AND LEARNING BY iCELL

We have used iCell as a teaching and learning tool for four courses; Life Sciences I for Biomedical Engineers, Medical Physics, Computational Modeling of Cellular Systems and Advanced Cardiac Electrophysiology, at the Joint Biomedical Engineering Program of University of Memphis and University of Tennessee.

Simulation-Based Teaching:

I have used iCell as a teaching tool when the course material covered the dynamics of cell membranes (e.g. action potential and the underlying ionic concentrations of calcium, potassium, sodium and chloride, and the ionic currents; ion channels, membrane pumps and exchangers). During my lectures, I run simulations with iCell to illustrate the electrical behavior of the cell membrane and the interactions between the ionic currents. I display simulations with different conditions to show the changes in the nonlinear behaviors of the cells. I also demonstrate to the students the significance of computational models and how the models can investigate more conditions than the experiments can since we can change the parameters and conditions numerically, and how the models can be used as predictive tools.

Simulation-Based Learning:

The students in my courses used iCell as a self-learning tool while they were assigned to do homework with it. The assigned homework had certain simulation protocols to run. The students were asked to write a report of their simulation results for the changes they observed for the assigned simulation protocols. For example, the following is a section from the homework assigned to the students taking the Advanced Cardiac Electrophysiology Course at the Joint Biomedical Engineering Program in October 2000.

Sample Sections: Homework Simulation Protocols for iCell Version 1a (Cardiac Modelbox)

Sinoatrial Node Cell Model (Figure 1)

1. Check the circuit representation for the currents that are present in the model.
2. Keep the default values, run the simulations and view the simulations for the voltage (V) and ionic currents for the control conditions.
3. Block I_{CaL} by 5%, 50% and by 100% (D600 block) and run the simulations for the transient results and steady state results.
4. Block I_{CaT} by 100% (Nickel block) and run simulations for the transient results and steady state results.
5. Block I_f by 100% (Cesium block) and run simulations for the transient results and steady state results.

Rabbit Atrial Cell Model

1. Check the circuit representation for the currents that are present in the model.
2. Keep the default values, run the simulations and view the simulations for V and ionic currents for the control conditions.
3. Block I_{CaL} by 50% and 100% (D600 block) and run the simulations for the transient results and steady state results.
4. Block I_t by 100% (4AP block) and run the simulations for the transient results and steady state results.
5. Stimulate the ventricular cell with a frequency of 1 (Control), 4, 5 and 6 Hz.

Guinea Pig Ventricular Cell Model

1. Check the circuit representation for the currents that are present in the model.
2. Keep the default values, run the simulations and view the simulations for V and ionic currents for the control conditions.
3. Block I_{Na} by 50% and by 100% (TTX block) and run the simulations for the transient results and steady state results.
4. Block I_{K1} by 100% (Barium block) and run simulations for the transient results and steady state results.
5. Stimulate the ventricular cell with a frequency of 1 (Control), 2, 3, 4, and 5 Hz.

Human Atrial Cell Model

1. Check the circuit representation for the currents that are present in the model.
2. Keep the default values, run the simulations and view the simulations for V and ionic currents for the control conditions.
3. Block I_t by 100% (4AP block) and run the simulations for the transient results and steady state results.

4. Block I_{sus} by 100% (TEA block) and run the simulations for the transient results and steady state results.
5. Block I_{Ks} by 100% (Propofol block) and run the simulations for the transient results and steady state results.
6. Block I_{Kr} by 100% (E4031 block) and run the simulations for the transient results and steady state results.

Simulation-Based Teaching, Learning and Collaboration Environment:

This modeling tool iCell was also used as a collaboration site among our colleagues interested in simulations of cell membrane activities. The iCell site has been used by many scientists and students (http://ssd1.bme.memphis.edu/icell/people.htm) from the fields of biosciences, engineering, life sciences and medical sciences in USA, Canada, China, Brazil, England, Ireland, the Netherlands, New Zealand, Spain and Turkey as a simulation-based teaching, learning and collaboration environment. Some professors from the following universities and disciplines requested permission to use iCell in their courses: Johns Hopkins University (Biomedical Engineering, Medical School), University of Utah (Bioengineering, Medical School), Texas A & M University (Bioengineering, Physiology and Pharmacology), California State Univ. Fullerton (Biological Sciences), Hope College (Biology), Kansas University Medical Center (Molecular and Integrative Physiology), Georgia University (Anatomy and Physiology, Nursing Anesthesia), University of Amsterdam (Cardiology, Physiology), University Hospital Groningen (Cardiology), University of Utrecht (Physiology), and Universitat de les Illes Balears (Animal Physiology).

IV. CONLCUSIONS

We are enhancing iCell by developing more applets for the Cardiac and Neuron Modelboxes. We are also adding more features to analyze the simulation results. One of our future goals is to use iCell for distance teaching. The platform-independent software, iCell, provides us with an interactive and user-friendly teaching, learning and collaboration environment for electrophysiology to be shared over the Internet. iCell will continue to motivate the development the students and scientists in the cross-disciplinary fields of engineering and life sciences in different parts of the world.

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REFERENCES

[1] Demir, S.S., Butera, R.J, DeFranceschi, A.A, Clark, J.W, and Byrne, J.H. Phase Sensitivity and Entrainment in a Modeled Bursting Neuron. *Biophysical Journal* 72: 579-594, 1997.

[2] Demir, S.S., Clark, J.W., Murphey, C.R. and Giles, W.R. A mathematical model of a rabbit sinoatrial node cell. *American Journal of Physiology* 266: C832-C852, 1994.

[3] Hodgkin, A.L. and Huxley, A.F. A quantitative description of membrane current and its application to conduction and excitation in nerve. *Journal of Physiology* 117: 500-544, 1952.

[4] Lindblad, D.S., Murphey, C.R., Clark, J.W. and Giles, W.R. A Model of the Action Potential and Underlying Membrane Currents in a Rabbit Atrial Cell. *American Journal of Physiology* 271: H1666-H1691, 1996.

[5] Luo, C.H. and Rudy, Y. A model of the ventricular cardiac action potential. *Circulation Research* 68: 1501-1526, 1991.

[6] Nygren, A., Fiset, C., Firek, L., Clark, J.W., Lindblad, D.S. and Giles, W.R. Mathematical Model of an Adult Human Atrial Cell The Role of K^+ Currents in Repolarization. *Circulation Research* 82: 63-81, 1998.

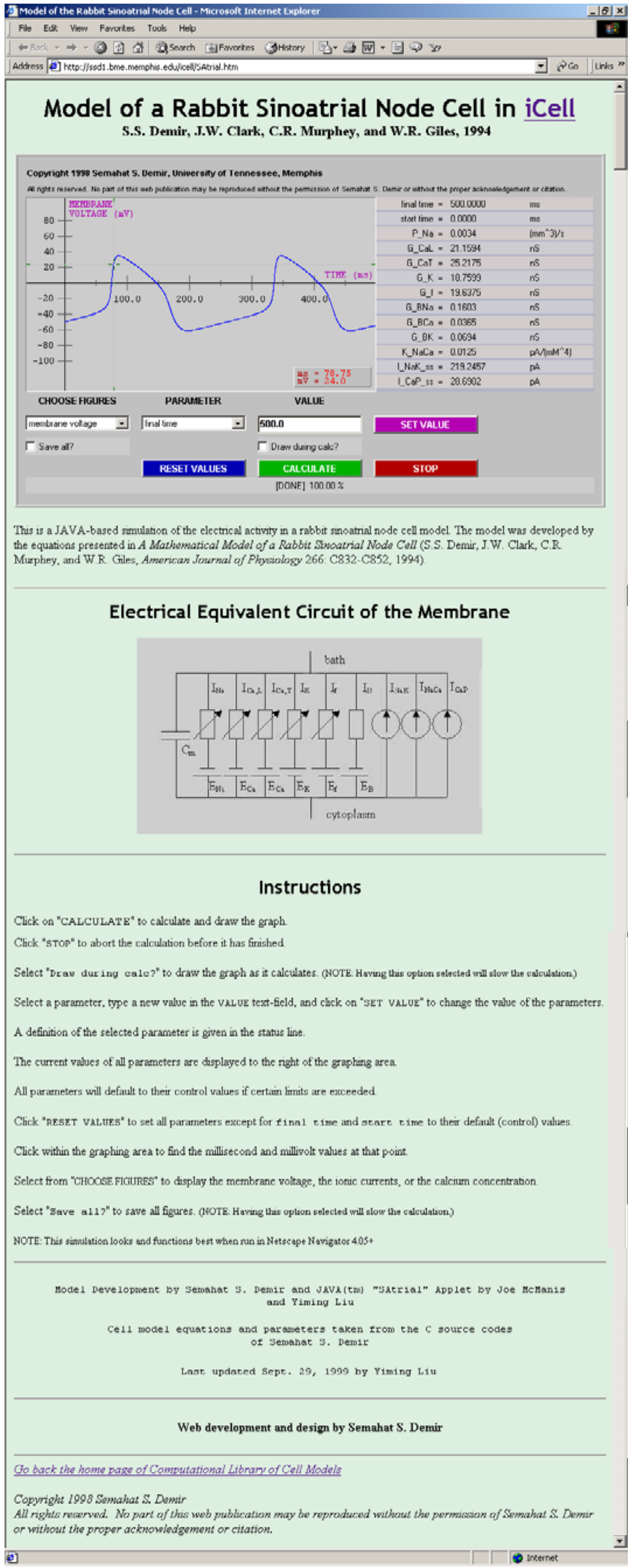

Figure 1: A sample JAVA applet from iCell